REMARKS

Claims 1, 3, 4, 11-19, 26, 29-33, and 51-69 are pending in the application.

In the present response Claim 3 has been canceled without prejudice or disclaimer; Claims 1, 4, 14, and 69 and have been amended; and Claims 70-72 have been added. Thus, Claims 1, 4, 11-19, 29-33, and 51-72 are now pending with Claims 1, 4, and 71 being independent Claims.

Claim 1 has been amended to more clearly express that which Applicants consider their invention and to remove the definition of the variable amino acids which are now included in the Replacement Sequence Listing submitted herewith. Claims 4 and 14 have been amended as suggested in the Office Action. Claim 69 has been amended to more clearly define that which Applicants consider their invention. As indicated below support for these changes is found in the specification as filed. No new matter is believed to be at issue.

New Claims 70-72 are supported in the specification as filed. For example at page 13, lines 15-17, and page 15, line 36- page 16, line 1. No new matter is believed to be at issue.

The sequence listing has been amended to identify the variable positions and to define the amino acid at position 294 as Xaa. Support for these changes is found in the Specification as filed, for example in page 41, line 18 through page 43, line 18 and in the enclosed Clustal alignment (Appendix A). According to the Specification as filed the consensus sequence of SEQ ID NO:66 was determined using a Clustal alignment of the polypeptides of the invention (see page 41, lines 18-20). No new matter is believed to be at issue.

According to the Office Action Claims 51-69 are withdrawn as being drawn to a non-elected invention. Applicants respectfully traverse. The polynucleotides of Claims 51-69 are within the scope of the consensus sequence and merely have defined amino acids at each of the positions where the consensus sequence has unsures. As stated in the Specification as filed, the polynucleotides of Claims 51-69 may be detected by the same nucleic acid probe. Rejoinder of Claims 51-69 is hereby kindly requested.

Specification

A replacement Sequence Listing is included herewith. This Sequence Listing includes the <223> identifier including the relevant information for the Xaa positions in SEQ ID NO:66. The amino acid sequence in SEQ ID NO:66 was amended at position 294 where Ile was replaced by Xaa. Support for these changes is found in the Specification as filed, at pages 41, line 13 through page 43, line 11. Further

more, as stated in the Specification as filed, the consensus sequence having the amino acid sequence of SEQ ID NO:66 was determined by aligning the amino acid sequences of the present invention using the Clustal alignment method (see page 13, lines 15-17). No new matter is believed to be at issue.

Page 42 of the Specification was amended to correctly identify the amino acids at positions 292, 293, and 329. As stated on page 13, lines 15-17 of the Specification as filed, "SEQ ID NO:66 is the amino acid sequence of the consensus sequence produced by the Megalign Program using the Clustal method and the amino acid sequences depicted in SEQ ID NOs:2, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 48, 55, 57, 59, and 61." Thus, to facilitate understanding of these changes, a Clustal alignment is included here as Appendix A. No new matter is believed to be at issue.

Claim Objections

Claim 4 has been amended to recite "wherein the nucleic acid does not have a nucleic acid sequence as set forth in SEQ ID NO:9" as suggested in the Office Action.

Claim Rejections

35 U.S.C. § 112, second paragraph

Claims 1 and 14 have been amended following the recommendations of the Office Action as follows:

Claim 1 has been amended as suggested on paragraph 8 of the Office Action to remove the word "fragment" from "the nucleic acid fragment".

Claim 1 has been amended to remove the definition of the variable amino acids since these are now defined in SEQ ID NO:66 of the Sequence Listing. An amended Sequence Listing is enclosed herewith.

Claim 14 has been amended to recite "wherein the second chimeric polynucleotide encodes a polypeptide comprising the maize C1 DNA binding domain, the maize transcription factor R, and the maize C1 activation domain". This change agrees with the understanding of the R region in the Office Action. The R region included consists of the entire coding region of the Lc allele of R (amino acids 1 through 160).

Removal of the 35 U.S.C. § 112, second paragraph rejections is kindly requested.

35 U.S.C. § 112, first paragraph

As seen below, no new matter was added to Claim 1 when adding the limitation during the response to the previous Office Action.

In the previous response Claim 1 was amended to add the limitation of Claim 4 as seen below. Before amendment Claim 1 was directed to an isolated nucleic acid

encoding a polypeptide with isoflavone synthase activity having the amino acid sequence of SEQ ID NO:66 wherein the Xaa positions are defined. Claim 4 is directed to an isolated nucleic acid encoding a polypeptide with isoflavone synthase activity wherein the nucleic acid does not have a nucleic acid sequence as set forth in SEQ ID NO:9. Thus, the amended Claim 1 introduced the limitations of the original Claim 4 to the original Claim 1. Thus, no new matter was introduced.

Furthermore, as stated in the MPEP 2163.05:

"To comply with the written descriptin requirement of 35U.S.C. 112, para. 1, or to be entitled to an earlier priority date or filing date under 35 U.S.C. 119, 120, or 365c, each claim limitation must be expressly, implicitly, or inherently supported in the originally filed disclosure."

And, in the MPEP 2163(b):

When an explicit limitation in a claim "is not present in the written description whose benefit is sought it must be shown that a person of ordinary skill would have understood, a the time the patent application was filed, that the description requires that limitation."

A person skilled in the art at the time of filing the application would have understood that the isolated nucleic acid of Claim 1 should not have the nucleic acid sequence shown in SEQ ID NO:9 for the reasons that follow.

The application was filed in the PCT with 50 claims. Claim 1 was directed to a nucleic acid encoding an isoflavone synthase having the amino acid sequence of SEQ ID NO:66. Claim 4 was directed to an isolated nucleic acid encoding an isoflavone synthase where the isolated nucleic acid does not have the nucleic acid sequence shown in SEQ ID NO:9. In the originally filed claims Applicants limited the isolated nucleic acid encoding an isoflavone synthase to not have the nucleotide sequence shown in SEQ ID NO:9, thus an isolated nucleic acid encoding an isoflavone synthase, SEQ ID NO: 66 for example, would not include the nucleotide sequence shown in SEQ ID NO:9.

Applicants respectfully request removal of the 35 U.S.C. § 112, first paragraph, new matter rejection.

Claim 3 has been canceled. Applicants respectfully submit that, at the time of filing, they had possession of the invention of Claim 4.

Applicants developed an assay to determine isoflavone synthase (IFS) activity in vitro (Examples 1 and 2), identified a soybean cDNA encoding IFS and demonstrated its functional activity (Examples 3-5), demonstrated that CYP93C1 has isoflavone synthase activity (Example 6), isolated cDNAs encoding isoflavone synthase from mung bean, red clover, white clover, lupine, snow pea, alfalfa, hairy

vetch, and lentil, assayed one each from mung bean, red clover, and snow pea for isoflavone synthase activity (Example 7), identified two different cDNAs encoding isoflavone synthases from a non-legume and determined that the amino acid sequence of all the isoflavone synthases identified were over 90% identical (Example 8), and identified the genomic DNA that encodes the soybean isoflavone synthase first tested (Example 16). The remaining examples in the specification describe alteration of isoflavone synthase activity in transgenic plants using nucleic acids of the invention. Thus, at the time of filing, Applicants had possession of the invention of Claim 4.

As mentioned above Applicants were the first to identify nucleic acid having isoflavone synthase activity and to show that the amino acid sequences of isoflavone synthases are very similar. It was surprising to Applicants that isoflavone synthases from non-legume species (sugarbeet) would be so similar to those from legume species. Thus, it is expected that all isoflavone synthases will be very similar.

Not all the isoflavone synthases disclosed in the specification appear to be of the same length. All of the sequences of the present invention may be as long as 521 amino acids. While the nucleic acids of those from white clover, lentil, hairy vetch, alfalfa, lupine, and sugarbeet (SEQ ID NOs:16, 18, 20, 22, 38, 40, 61, 55, 57, 59, and 48) are not as long, they were amplified a second time with primers corresponding to nucleic acids that encode amino acids 1-9 and 514-521 of SEQ ID NO:2. These regions of SEQ ID NOs:16, 18, 20, 22, 38, 40, 61, 55, 57, 59, and 48 were not sequenced in the nucleic acids obtained from such amplifications. Nonetheless, since the primers of SEQ ID NO: 2 were used to amplify SEQ ID NOs:16, 18, 20, 22, 38, 40, 61, 55, 57, 59, and 48, one skilled in the art would expect the sequences of all of these SEQ ID NOS to be similar to SEQ ID NO: 2. Thus, there is sufficient written description of the nucleic acids in Claim 4.

As stated in the first full-paragraph of page 8 of the Office Action, sufficient written description of a genus of polypeptides may be achieved by a recitation of a representative number of polypeptides defined by their amino acid sequence. There are polypeptides corresponding to 20 different isoflavone synthases described in the specification. The polypeptides have been isolated from legume and non-legume plants, thus there is sufficient description of a genus of polypeptides in the application as filed.

Applicants obtained nucleic acids encoding isoflavone synthases from legume and non-legume plants using the same pair of primers. When Applicants isolated nucleic acids encoding isoflavone synthases from non-legume species they compared the nucleotide and amino acid sequences with those of the soybean isoflavone synthase having SEQ ID NOs:1 and 2 and determined that the nucleotide

sequences are no less than 91.9% identical and the amino acid sequences are no less than 95.6% identical (see Table 2, pages 41 and 42 of the Specification as filed). Thus, the claimed invention is adequately described in the Specification as filed.

The specification teaches a method for determining isoflavone synthase activity of a polypeptide. The specification also teaches the nucleotide and amino acid sequences of 20 different isoflavone synthases identified in 5 different legumes and one non-legume. Thus, following the teachings of the Specification, undue experimentation would not be required of one of skill in the art to determine which isolated nucleic acids encode polypeptides have isoflavone synthase activity. The full scope of the claimed invention is enabled in the Specification as filed.

Removal of the 35 U.S.C. § 112, first paragraph rejections is respectfully requested.

35 U.S.C. § 102 (a) and (b)

The declaration by Dr. Brian McGonigle, submitted with the communication filed 12/15/03 is submitted here signed by Gary Fader, Woosuk Jung, Joan Odell, Oliver Yu, and Brian McGonigle. This 35 U.S.C. § 102 (a) rejection is now considered unnnecessary.

35 U.S.C. § 102 (b)

By virtue of the cancellation of Claim 3 Siminszki et al. is no longer a 102 reference. Furthermore there are many P450 monooxygenases that carry out many different functions. Identifying the particular P450 monooxygenase involved in isoflavone synthesis could not have been determined without experimentation. Removal of the 35 U.S.C. § 102(b) rejection is respectfully requested.

35 U.S.C. § 103

By virtue of the cancellation of Claim 3, the language of amended Claim 4, and the presentation of the Declaration by Dr. Brian McGonigle now signed by all the inventors Siminszki et al. is no longer an applicable reference. Removal of the 35 U.S.C. § 103 rejection is respectfully requested.

In view of the foregoing, allowance of the above-referenced application is respectfully requested.

Respectfully submitted,

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Dated: Sept. 10, 2004

APPENDIX A (Continued)

Clustal V alignment of the amino acid sequences corresponding to isoflavone synthases from soybean (SEQ ID NO:2 and SEQ ID NO:10), alfalfa (SEQ ID NO:16, SEQ ID NO:57, and SEQ ID NO:59), hairy vetch (SEQ ID NO:18), lentil (SEQ ID NO:20 and SEQ ID NO:22), mung bean (SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, and SEQ ID NO:30), red clover (SEQ ID NO:32 and SEQ ID NO:34), snow pea (SEQ ID NO:36), white clover (SEQ ID NO:38 and SEQ ID NO:40), sugar beet (SEQ ID NO:48 and SEQ ID NO:61), lupine (SEQ ID NO:55), and the consensus sequence (SEQ ID NO:66). Amino acids that are different in at least one sequence are boxed in black and written in white. The program uses dashes to maximize the alignment.

```
                1                                                          60
SEQ ID NO:2     MLLELALGL F VLALF L HLRPTP S A K SKALRHLPNPPSP K PRLPFIGH L HLLKDKLLHYA L
SEQ ID NO:16    --------- - ----F L HLRPTP S A K SKALRHLPNPPSP K PRLPFIGH L HLLKDKLLHYA L
SEQ ID NO:18    --------- - ----F L HLRPTP T A K SKALRHLPNPPSP K PRLPFIGH L HLLKDKLLHYA L
SEQ ID NO:20    --------- - ----F L HLRPTP T A K SKALRHLPNPPSP K PRLPFIGH P HLLKDKLLHYA L
SEQ ID NO:22    --------- - ----F L HLRPTP T A K SKALRHLPNPPSP K PRLPFIGH L HLLKDKLLHYA L
SEQ ID NO:24    MLLELALGL L VLALF L HLRPTP T A K SKALRHLPNPPSP K PRLPFIGH L HLLKDKLLHYA L
SEQ ID NO:26    MLLELALGL L VLALF L HLRPTP T A K SKALRHLPNPPSP K PRLPFIGH L HLLKDKLLHYA L
SEQ ID NO:28    MLLELALGL L VLALF L HLRPTP T A K SKALRHLPNPPSP K PRLPFIGH L HLLKDKLLHYA L
SEQ ID NO:30    MLLELALGL L VLALF L HLRPTP T A K SKALRHLPNPPSP K PRLPFIGH L HLLKDKLLHYA L
SEQ ID NO:32    MLLELALGL L VLALF L HLRPTP T A K SKALRHLPNPPSP K PRLPFIGH L HLLKDKLLHYA L
SEQ ID NO:34    MLLELALGL L VLALF L HLRPTP T A K SKALRHLPNPPSP K PRLPFIGH L HLLKDKLLHYA L
SEQ ID NO:36    MLLELALGL F VLALF L HLRPTP S A K SKALRHLPNPPSP K PRLPFIGH L HLLKDKLLHYA L
SEQ ID NO:38    --------- - ----- S HLRPTP S A I SKALRHLPNPPSP R PRLPFIGH L HLLKDKLLHYA P
SEQ ID NO:40    --------- - ----F L HLRPTP T A K SKALRHLPNPPSP K PRLPFIGH L HLLKDKLLHYA L
SEQ ID NO:48    --------- - ----- L HLRPTP T A K SKALRHLPNPPSP K PRLPFIGH L HLLKDKLLHYA L
SEQ ID NO:55    --------- - ----F L HLRPTP T A K SKALRHLPNPPSP K PRLPFIGH L HLLKDKLLHYA L
SEQ ID NO:57    --------- - ----F L HLRPTP T A K SKALRHLPNPPSP K PRLPFIGH L HLLKDKLLHYA L
SEQ ID NO:59    --------- - ----F L HLRPTP T A K SKALRHLPNPPSP K PRLPFIGH L HLLKDKLLHYA L
SEQ ID NO:61    --------- - ----F L HLRPTP T A K SKALRHLPNPPSP K PRLPFIGH L HLLKDKLLHYA L
SEQ ID NO:66    MLLELALGL X VLALF X HLRPTP X A X SKALRHLPNPPSP X PRLPFIGH X HLLKDKLLHYA X
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APPENDIX A (Continued)

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                    61                                                                      120
SEQ ID NO: 2   IDLSKKHGPLFS LS FGSMPTVVASTPELFKLFLQ TH EATSF N TRFQTSA I R R LTYD NS VA
SEQ ID NO:16   IDLSKKHGPLFS LS FGSMPTVVASTPELFKLFLQ TH EATSF N TRFQTSA T R R LTYD NS VA
SEQ ID NO:18   IDLSKKHGPLFS LY FGSMPTVVASTPELFKLFLQ TH EATSF N TRFQTSA I R R LTYD SL VA
SEQ ID NO:20   IDLSKKHGPLFS LY FGSMPTVVASTPELFKLFLQ TH EATSF N TRFQTSA I R R LTYD SS VA
SEQ ID NO:22   IDLSKKHGPLFS LY FGSMPTVVASTPELFKLFLQ TH EATSF N TRFQTSA I R R LTYD SS VA
SEQ ID NO:24   IDLSKKHGPLFS LY FGSMPTVVASTPELFKLFLQ TH EATSF N TRFQTSA I R R LTYD SS VA
SEQ ID NO:26   IDLSKKHGPLFS LY FGSMPTVVASTPELFKLFLQ TH EATSF N TRFQTSA I R R LTYD SS VA
SEQ ID NO:28   IDLSKKHGPLFS LY FGSMPTVVASTPELFKLFLQ TH EATSF N TRFQTSA I R R LTYD SS VA
SEQ ID NO:30   IDLSKKHGPLFS LY FGSMPTVVASTPELFKLFLQ TH EATSF N TRFQTSA I R R LTYD SS VA
SEQ ID NO:32   IDLSKKHGPLFS LY FGSMPTVVASTPELFKLFLQ TH EATSF N TRFQTSA I R R LTYD SS VA
SEQ ID NO:34   IDLSKKHGPLFS LY FGSMPTVVASTPELFKLFLQ TH EATSF N TRFQTSA I R R LTYD SS VA
SEQ ID NO:36   IDLSKKHGPLFS LS FGSMPTVVASTPELFKLFLQ AH EATSF S TRFQTSA V R R LTYD NS VA
SEQ ID NO:38   IDLSKKHGPLFS LS FGSMPTVVASTPELFKLFLQ TH EATSF N TRFQTSA I R H LTYD NS VA
SEQ ID NO:40   IDLSKKHGPLFS LY FGSMPTVVASTPELFKLFLQ TH EATSF N TRFQTSA I R R LTYD NS VA
SEQ ID NO:48   IDLSKKHGPLFS HY FGSMPTVVASTPELFKLFLQ TN EATSF N TRFQTSA I R R LTYD SS VA
SEQ ID NO:55   IDLSKKHGPLFS LY FGSMPTVVASTPELFKLFLQ TH EATSF N TRFQTSA I R R LTYD SS VA
SEQ ID NO:57   IDLSKKHGPLFS LY FGSMPTVVASTPELFKLFLQ TH EATSF N TRFQTSA I R R LTYD SS VA
SEQ ID NO:59   IDLSKKHGPLFS LY FGSMPTVVASTPELFKLFLQ TH EATSF N TRFQTSA I R R LTYD SS VA
SEQ ID NO:61   IDLSKKHGPLFS LY FGSMPTVVASTPELFKLFLQ TH EATSF N TRFQTSA I R R LTYD SS VA
SEQ ID NO:66   IDLSKKHGPLFS XX FGSMPTVVASTPELFKLFLQ XX EATSF X TRFQTSA X R X LTYD XX VA
```
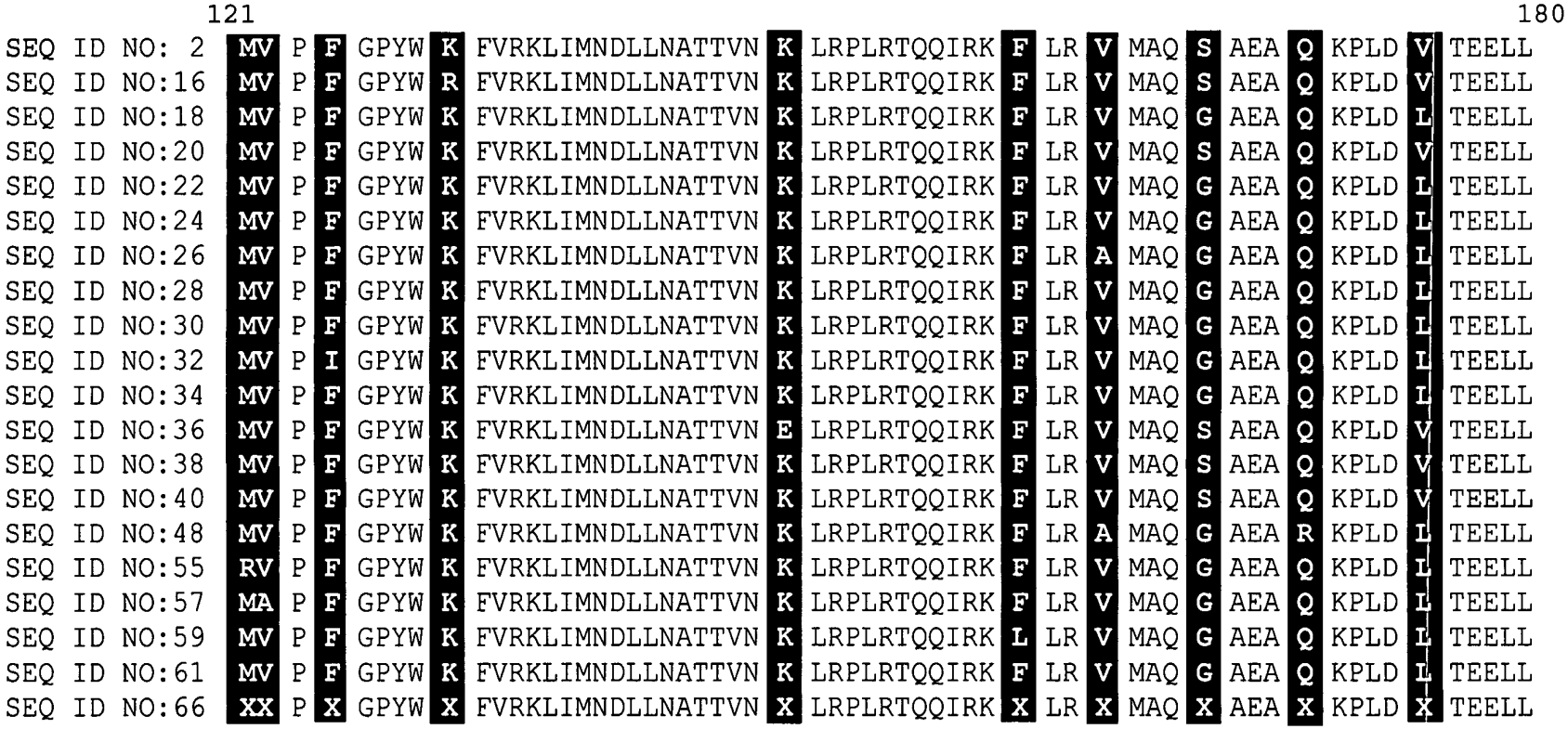

APPENDIX A (Continued)



APPENDIX A (Continued)

	181													240
SEQ ID NO: 2	KW	T	NST	I	SMM	M	LGEAEEIRDIAREVLKI	F	GEYSLTDFI	W	PLK	Y	LKVGKYEKRIDDILNKF	
SEQ ID NO:16	KW	T	NST	I	SMM	M	LGEAEEIRDIAREVLKI	F	GEYSLTDFI	W	PLK	Y	LKVGKYEKRIDDILNKF	
SEQ ID NO:18	KW	T	NST	I	SMM	M	LGEAEEIRDIAREVLKI	Y	GEYSLTDFI	W	PLK	H	LKVGKYEKRIDDILNKF	
SEQ ID NO:20	KW	T	NST	I	SMM	M	LGEAEEIRDIAREVLKI	F	GEYSLTDFI	W	PLK	Y	LKVGKYEKRIDDILNKF	
SEQ ID NO:22	KW	T	NST	I	SMM	V	LGEAEEIRDIAREVLKI	F	GEYSLTDFI	W	PLK	H	LKVGKYEKRIDDILNKF	
SEQ ID NO:24	KW	T	NST	I	SMM	M	LGEAEEIRDIAREVLKI	F	GEYSLTDFI	W	PLK	H	LKVGKYEKRIDDILNKF	
SEQ ID NO:26	KW	T	NST	I	SMM	M	LGEAEEIRDIAREVLKI	F	GEYSLTDFI	W	PLK	H	LKVGKYEKRIDDILNKF	
SEQ ID NO:28	KW	T	NST	I	SMM	M	LGEAEEIRDIAREVLKI	F	GEYSLTDFI	W	PLK	H	LKVGKYEKRIDDILNKF	
SEQ ID NO:30	KW	T	NST	I	SMM	M	LGEAEEIRDIAREVLKI	F	GEYSLTDFI	W	PLK	H	LKVGKYEKRIDDILNKF	
SEQ ID NO:32	KW	T	NST	I	SMM	M	LGEAEEIRDIAREVLKI	F	GEYSLTDFI	W	PLK	H	LKVGKYEKRIDDILNKF	
SEQ ID NO:34	KW	T	NST	I	SMM	M	LGEAEEIRDIAREVLKI	F	GEYSLTDFI	W	PLK	H	LKVGKYEKRIDDILNKF	
SEQ ID NO:36	KW	T	NST	I	SMM	M	LGEAEEIRDIAREVLKI	F	GEYSLTDFI	W	PLK	Y	LKVGKYEKRIDDILNKF	
SEQ ID NO:38	KW	T	NST	I	SMM	M	LGEAEEIRDIAREVLKI	F	GEYSLTDFI	W	PLK	Y	LKVGKYEKRIDDILNKF	
SEQ ID NO:40	KW	T	NST	I	SMM	M	LGEAEEIRDIAREVLKI	F	GEYSLTDFI	W	PLK	Y	LKVGKYEKRIDDILNKF	
SEQ ID NO:48	KW	A	NST	I	SMM	M	LGEAEEIRDIAREVLKI	F	GEYSLTDFI	W	PLK	H	LKVGKYEKRIDDILNKF	
SEQ ID NO:55	KW	T	NST	I	SMM	M	LGEAEEIRDIAREVLKI	F	GEYSLTDFI	W	PLK	H	LKVGKYEKRIDDILNKF	
SEQ ID NO:57	KW	T	NST	T	SMM	M	LGEAEEIRDIAREVLKI	F	GEYSLTDFI	R	PLK	H	LKVGKYEKRIDDILNKF	
SEQ ID NO:59	KW	T	NST	I	SMM	M	LGEAEEIRDIAREVLKI	F	GEYSLTDFI	W	PLK	H	LKVGKYEKRIDDILNKF	
SEQ ID NO:61	KW	T	NST	I	SMM	M	LGEAEEIRDIAREVLKI	F	GEYSLTDFI	W	PLK	H	LKVGKYEKRIDDILNKF	
SEQ ID NO:66	KW	X	NST	X	SMM	X	LGEAEEIRDIAREVLKI	X	GEYSLTDFI	X	PLK	X	LKVGKYEKRIDDILNKF	

APPENDIX A (Continued)

	241													300
SEQ ID NO: 2	DPVVERVIKKRR	E	IVRRR	K	NGE	VV	EGE	A	SGV	F	LDTLLEFAEDET	M	EIKITK	EQI	KGLVVD
SEQ ID NO:16	DPVVERVIKKRR	G	IVRRR	E	NGE	VV	EGE	A	SGV	F	LDTLLEFAEDET	M	EIKITK	EQI	KGLVVD
SEQ ID NO:18	DPVVERVIKKRR	E	IVRRR	K	NGE	VV	EGE	V	SGV	F	LDTLLEFAEDET	T	EIKITK	DHI	KGLVVD
SEQ ID NO:20	DPVVERVIKKRR	E	IVRRR	K	NGE	VV	EGE	A	SGV	F	LDTLLEFAEDET	M	EIKITK	EQI	KGLVVD
SEQ ID NO:22	DPVVERVIKKRR	E	IVRRR	K	NGE	VV	EGE	V	SGV	F	LDTLLEFAEDET	M	EIKITK	DHI	KGLVVD
SEQ ID NO:24	DPVVERVIKKRR	E	IVRRR	K	NGE	VV	EGE	V	SGV	F	LDTLLEFAEDET	M	EIKITK	DHI	KGLVVD
SEQ ID NO:26	DPVVERVIKKRR	E	IVRRR	K	NGE	VV	EGE	V	SGV	F	LDTLLEFAEDET	M	EIKITK	DHI	KGLVVD
SEQ ID NO:28	DPVVERVIKKRR	E	IVRRR	K	NGE	VV	EGE	V	SGV	F	LDTLLEFAEDET	T	EIKITK	DHI	KGLVVD
SEQ ID NO:30	DPVVERVIKKRR	E	IVRRR	K	NGE	VV	EGE	V	SGV	F	LDTLLEFAEDET	M	EIKITK	DHI	KGLVVD
SEQ ID NO:32	DPVVERVIKKRR	E	IVRRR	K	NGE	VD	EGE	V	SGV	F	LDTLLEFAEDET	T	EIKITK	DHI	KGLVVD
SEQ ID NO:34	DPVVERVIKKRR	E	IVRRR	K	NGE	VV	EGE	V	SGV	F	LDTLLEFAEDET	T	EIKITK	DHI	KGLVVD
SEQ ID NO:36	DPVVERVIKKRR	E	IVRRR	K	NGE	VV	EGE	A	SGV	F	LDTLLEFAEDET	M	EIKITK	EQI	KGLVVD
SEQ ID NO:38	DPVVERVIKKRR	E	IVRRR	K	NGE	VV	EGE	A	SGV	F	LDTLLEFAEDET	M	EIKITK	EQI	KGLVVD
SEQ ID NO:40	DPVVERVIKKRR	E	IVRRR	K	NGE	VV	EGE	A	SGV	F	LDTLLEFAEDET	M	EIKITK	EQI	KGLVVD
SEQ ID NO:48	DPVVERVIKKRR	E	IVRRR	K	NGE	VV	EGE	V	SGV	F	LDTLLEFAEDET	M	EIKITK	DHT	KGLVVD
SEQ ID NO:55	DPVVERVIKKRR	E	IVRRR	K	NGE	VV	EGE	V	SGV	L	LDTLLEFAEDET	M	EIKITK	DHI	KGLVVD
SEQ ID NO:57	DPVVERVIKKRR	E	IVRRR	K	NGE	VV	EGE	V	SGV	F	LDTLLEFAEDET	T	EIKITK	DHI	KGLVVD
SEQ ID NO:59	DPVVERVIKKRR	E	IVRRR	K	NGE	VI	EGE	V	SGV	F	LDTLLEFAEDET	T	EIKITK	DHI	KGLVVD
SEQ ID NO:61	DPVVERVIKKRR	E	IVRRR	K	NGE	DV	EGE	V	SGV	F	LDTLLEFAEDET	M	EIKITK	DHI	KGLVVD
SEQ ID NO:66	DPVVERVIKKRR	X	IVRRR	X	NGE	XX	EGE	X	SGV	X	LDTLLEFAEDET	X	EIKITK	XXX	KGLVVD

APPENDIX A (Continued)

	301														360
SEQ ID NO: 2	F	FSAG	T	DSTA	VA	TEWALAELINNP	R	VL	QK	AREE	V	YSVVGKD	R	LVDEVDTQNLPYIRAIVK	
SEQ ID NO:16	L	FSAG	T	DSTA	VA	TEWALAELINNP	R	VL	QK	AREE	V	YSVVGKD	R	LVDEVDTQNLPYIRAIVK	
SEQ ID NO:18	F	FSAG	I	DSTA	VA	TEWALAELINNP	K	VL	EK	AREE	V	YSVVGKD	R	LVDEVDTQNLPYIRAIVK	
SEQ ID NO:20	F	FSAG	T	DSTA	VA	TEWALAELINNP	R	VL	QK	AREE	V	YSVVGKD	I	LVDEVDTQNLPYIRAIVK	
SEQ ID NO:22	F	FSAG	T	DSTA	VA	TEWALAELINNP	K	VL	EK	AREE	V	YSVVGKD	R	LVDEVDTQNLPYIRAIVK	
SEQ ID NO:24	F	FSAG	T	DSTA	VA	TEWALAELINNP	K	VL	EK	AREE	A	YSVVGKD	R	LVDEVDTQNLPYIRAIVK	
SEQ ID NO:26	F	FSAG	T	DSTA	VA	TEWALAELINNP	K	VL	EK	AREE	V	YSVVGKD	R	LVDEVDTQNLPYIRAIVK	
SEQ ID NO:28	F	FSAG	T	DSTA	VA	TEWALAELINNP	K	VL	EK	AREE	V	YSVVGKD	R	LVDEVDTQNLPYIRAIVK	
SEQ ID NO:30	F	FSAG	T	DSTA	EA	TEWALAELINNP	K	VL	EK	AREE	V	YSVVGKD	R	LVDEVDTQNLPYIRAIVK	
SEQ ID NO:32	F	FSAG	T	DSTA	VA	TEWALAELINNP	K	VL	EK	AREE	V	YSVVGKD	R	LVDEVDTQNLPYIRAIVK	
SEQ ID NO:34	F	FSAG	T	DSTA	VA	TEWALAELINNP	K	VL	EK	AREE	V	YSVVGKD	R	LVDEVDTQNLPYIRAIVK	
SEQ ID NO:36	F	FSAG	T	DSTA	VA	TEWALAELINNP	R	VL	QK	AREE	V	YSVVGKD	R	LVDEVDTQNLPYIRAIVK	
SEQ ID NO:38	F	FSAG	T	DSTA	VV	TEWALAELINNP	R	VL	QK	AREE	V	YSVVGKD	R	LVDEVDTQNLPYIRAIVK	
SEQ ID NO:40	F	FSAG	T	DSTA	VA	TEWALAELINNP	K	VL	QK	AREE	A	YSVVGKD	R	LVDEVDTQNLPYIRAIVK	
SEQ ID NO:48	F	FSAG	T	DSTA	VA	TEWALAELINNP	K	VL	EK	AREE	V	YSVVGKD	R	LVDEVDTQNLPYIRAIVK	
SEQ ID NO:55	F	FSAG	T	DSTA	VA	TEWALAELINNP	K	VL	ER	AREE	V	YSVVGKD	R	LVDEVDTQNLPYIRAIVK	
SEQ ID NO:57	F	FSAG	T	DSTA	VA	TEWALAELINNP	K	VL	EK	AREE	V	YSVVGKD	R	LVDEVDTQNLPYIRAIVK	
SEQ ID NO:59	F	FSAG	T	DSTA	VA	TEWALAELINNP	K	VL	EK	AREE	V	YSVVGKD	R	LVDEVDTQNLPYIRAIVK	
SEQ ID NO:61	F	FSAG	T	DSTA	VA	TEWALAELINNP	K	VL	EK	AREE	V	YSVVGKD	R	LVDEVDTQNLPYIRAIVK	
SEQ ID NO:66	X	FSAG	X	DSTA	XX	TEWALAELINNP	X	VL	XX	AREE	X	YSVVGKD	X	LVDEVDTQNLPYIRAIVK	

APPENDIX A (Continued)

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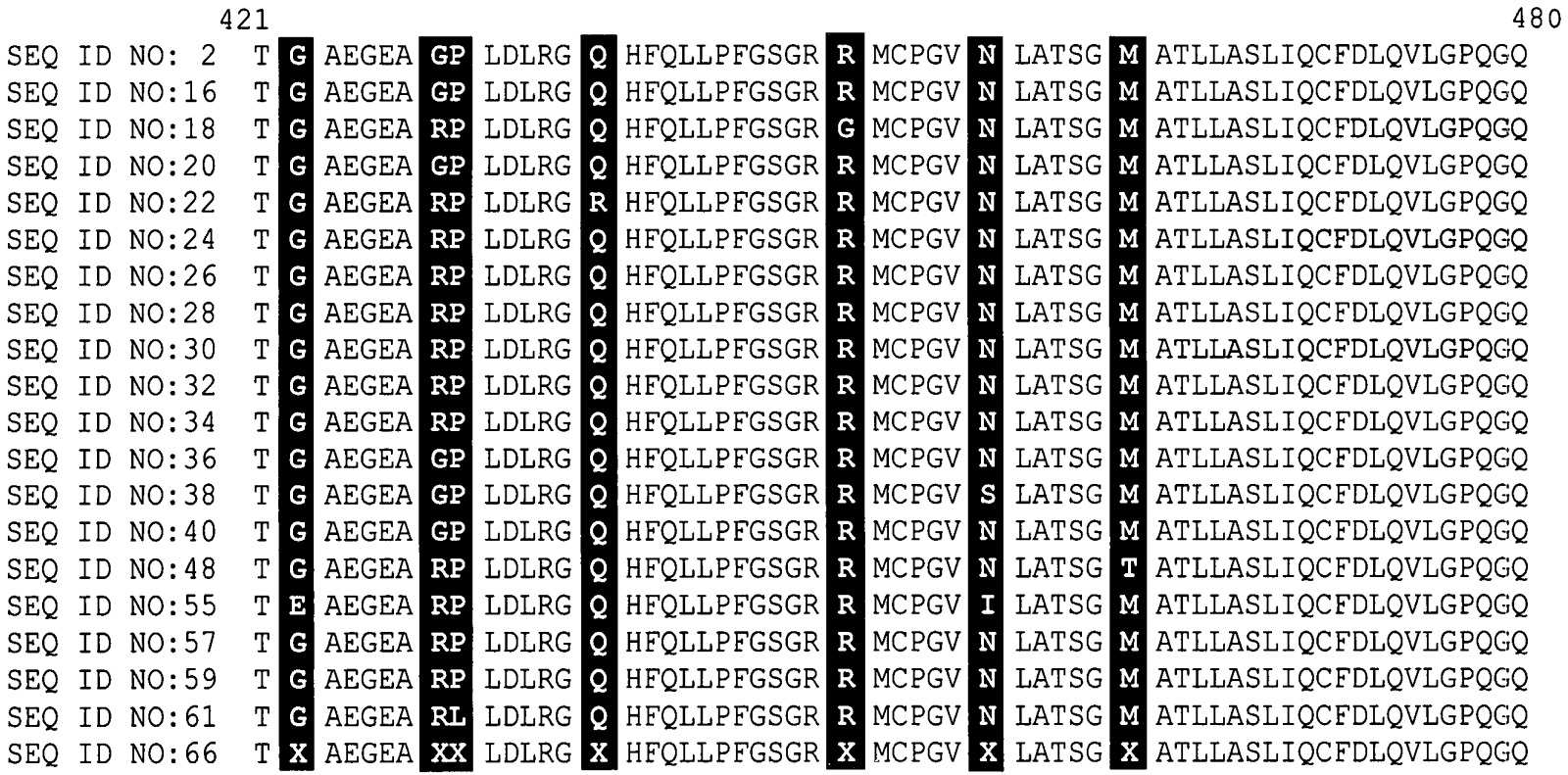
                  361                                                                                  420
SEQ ID NO: 2   ETFRMHPPLPVVKRKC T EEC E ING Y V I PEGAL VL FNVWQVG R D P KYWDRPSE F RPERFLE
SEQ ID NO:16   ETFRMHPPLPVVKRKC T EEC E ING Y V I PEGAL VL FNVWQVG R D P KYWDRPSE F RPERFLE
SEQ ID NO:18   ETFRMHPPLPVVKRKC T EEC E ING Y V I PEGAL IL FNVWQVG R D P KYWDRPSE F RPERFLE
SEQ ID NO:20   ETFRMHPPLPVVKRKC T EEC E ING H V I PEGAL VL FNVWQVG R D P KYWDRPSE F RPERFLE
SEQ ID NO:22   ETFRMHPPLPVVKRKC T EEC E ING C V T PEGAL IL FNVWQVG R D P KYWDRPSE F RPERFLE
SEQ ID NO:24   ETFRMHPPLPVVKRKC T EEC E ING Y V I PEGAL IL FNVWQVG R D P KYWDRPSE F RPERFLE
SEQ ID NO:26   ETFRMHPPLPVVKRKC T EEC E ING Y V I PEGAL IL FNVWQVG R D P KYWDRPSE F RPERFLE
SEQ ID NO:28   ETFRMHPPLPVVKRKC T EEC E ING Y V I PEGAL IL FNVWQVG R D P KYWDRPSE F RPERFLE
SEQ ID NO:30   ETFRMHPPLPVVKRKC T EEC E ING Y V I PEGAL IL FNVWQVG R D P KYWDRPSE F RPERFLE
SEQ ID NO:32   ETFRMHPPLPVVKRKC T EEC E ING Y V I PEGAL IL FNVWQVG R D P KYWDRPSE F RPERFLE
SEQ ID NO:34   ETFRMHPPLPVVKRKC T EEC E ING Y V I PEGAL IL FNVWQVG R D P KYWDRPSE F RPERFLE
SEQ ID NO:36   ETFRMHPPLPVVKRKC T EEC E ING Y V I PEGAL VL FNVWQVG K D P KYWDRPSE F RPERFLE
SEQ ID NO:38   ETFRMHPPLPVVKRKC T EEC E ING Y V I PEGAL VL FNVWQVG R D P KYWDRPSE S RPERFLE
SEQ ID NO:40   ETFRMHPPLPVVKRKC T EEC G ING Y V I PEGAL VL FNVWQVG R D P KYWDRPSE F RPERFLE
SEQ ID NO:48   ETFRMHPPLPVVKRKC T EEC E ING Y V I PEGAL IP FNVWQVG R D P KYWDRPSE F RPERFLE
SEQ ID NO:55   ETFRMHPPLPVVKRKC T EEC E ING Y V I PEGAL IL FNVWQVG R D P KYWDRPSE F RPERFLE
SEQ ID NO:57   ETFRMHPPLPVVKRKC T EEC E ING Y V I PEGAL IL FNVWQVG R D S KYWDRPSE F RPERFLE
SEQ ID NO:59   ETFRMHPPLPVVKRKC T EEC E ING Y V I PEGAL IL FNVWQVG R D P KYWDRPSE F RPERFLE
SEQ ID NO:61   ETFRMHPPLPVVKRKC I EEC E ING Y V I PEGAL IL FNVWQVG R D P KYWDRPSE F RPERFLE
SEQ ID NO:66   ETFRMHPPLPVVKRKC X EEC X ING X V X PEGAL XX FNVWQVG X D X KYWDRPSE X RPERFLE
```

APPENDIX A (Continued)



APPENDIX A (Continued)

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                481                                                 522
SEQ ID NO: 2    ILKG D DAKVSMEERAGLTVPRAHSLVCVPLARIGVASKLLS-
SEQ ID NO:16    ILKG D DAKVSMEERAGLTVPRAHSLVCVPLARI---------
SEQ ID NO:18    ILKG G DAKVSMEERAGLTVPRAHSLVCVPLARI---------
SEQ ID NO:20    ILKG D DAKVSMEERAGLTVPRAHSLVCVPLARI---------
SEQ ID NO:22    ILKG G DAKVSMEERAGLTVPRAHSLVCVPLARI---------
SEQ ID NO:24    ILKG G DAKVSMEERAGLTVPRAHSLVCVPLARIGVASKLLSK
SEQ ID NO:26    ILKG G DAKVSMEERAGLTVPRAHSLVCVPLARIGVASKLLS-
SEQ ID NO:28    ILKG G DAKVSMEERAGLTVPRAHSLVCVPLARIGVASKLLS-
SEQ ID NO:30    ILKG G DAKVSMEERAGLTVPRAHSLVCVPLARIGVASKLLS-
SEQ ID NO:32    ILKG G DAKVSMEERAGLTVPRAHSLVCVPLARIGVASKLLS-
SEQ ID NO:34    ILKG G DAKVSMEERAGLTVPRAHSLVCVPLARIGVASKLLS-
SEQ ID NO:36    ILKG D DAKVSMEERAGLTVPRAHSLVCVPLARIGVASKLLS-
SEQ ID NO:38    ILKG D DAKVSMEERAGLTVPRAHSLVCVPLARI---------
SEQ ID NO:40    ILKG D DAKVSMEERAGLTVPRAHSLVCVPLARI---------
SEQ ID NO:48    ILKG G DAKVSMEERAGLTVPRAHSLVCVPLARI---------
SEQ ID NO:55    ILKG G DAKVSMEERAGLTVPRAHSLVCVPLARI---------
SEQ ID NO:57    ILKG G DAKVSMEERAGLTVPRAHSLVCVPLARI---------
SEQ ID NO:59    ILKG G DAKVSMEERAGLTVPRAHSLVCVPLARI---------
SEQ ID NO:61    ILKG G DAKVSMEERAGLTVPRAHSLVCVPLARI---------
SEQ ID NO:66    ILKG X DAKVSMEERAGLTVPRAHSLVCVPLARIGVASKLLS-
```